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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/507,146 | 02/18/2000 | Walter Newman | L0559/7001(ERP) | 8881 |

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| EXAMINER | |
|---|---|
| CANELLA, KAREN A | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1642 | |

DATE MAILED: 05/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/507,146 | NEWMAN ET AL. | |
| | Examiner | Art Unit | |
| | Karen A Canella | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☐ Claim(s) 1,10,11,15,20-24,34,41-55 and 59-65 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) 1,10,11,15,20-24,34,41-55 and 59-65 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

1. Claims 6 and 7 have been canceled. Claims 59-65 have been added. Claims 1, 10, 11, 15, 20-24, 34, 41-55 and 59-65 are pending an under consideration.

2. Text of sections of Title 35 US Code not provided in this action can be found in a previous action.

3. Claims 45 and 63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 45 and 63 are rendered vague and indefinite by the recitation of "the chemokines of Table 1" Section 2173.05(s) of the MPEP states
"Where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience. Ex parte Fressola, 27 USPQ2d 1608, 1609 (Bd. Pat. App. & Inter. 1993) (citations omitted)".

4. Claims 10, 11, 59 and 60 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. .

The instant rejected claims are drawn to compositions and pharmacological compositions comprising chemokines. Claims 10 and 59 have the specific limitation of chemokines having agonists activity; claims 11 and 60 have the specific limitation of chemokines having antagonist activity. Thus, the claims drawn to a genus of "chemokines" include chemokines having agonistic or antagonistic activities. The specification teaches that "truncation or deletion of the highly basic carboxyl terminal of chemokines can be used to create novel chemokine agonists

having improved half-life characteristics" (page 5, lines 11-13). The specification further states that "truncated or elongated chemokine peptides, in particular, at the amino terminus" can be used to inhibit the normal pharmacological activity of the chemokine (page 15, lines 4-16), and thus be a chemokine antagonist. The specification contemplates all families of chemokines as part of the instant invention (page 1). The specification fails to provide a structure for any chemokine which was altered at the amino terminus to produce a chemokine "antagonist". The specification does not provide a single structure of a truncated chemokine which serves as an agonist chemokine. The disclosure of the composition comprising a chemokine covalently coupled to biotin does not adequately describe the genus of agonistic and antagonists chemokines claimed.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) . are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative

number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

It is noted that the instant claims encompassing agonists and antagonists of chemokines are not limited in structure by the general discussion of chemokine agonists and antagonists on page 5.

5. Claims 1, 10, 11, 15, 20-24, 34, 41-55 and 59-65 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention..

The instant claims are drawn to a composition comprising a biotin conjugated to a chemokine and an anti-biotin antibody. the specification teaches that the complex comprising the anti-biotin antibodies and the biotin-chemokine conjugate ahs a half-life which is significantly greater than the half life of the free chemokine or biotintylated chemokine (page 5, lines 25-28), and that the half-life is on the order of from about one day to one month (page 5, lines 30-31).

The art teaches that while the presence of the Fc antibody domain confers an increased half-life in vivo to antibodies and fusion proteins comprising said domain, formation of the antibody-antigen complex results in the rapid elimination of the complex from the circulation. Schechter et al (US 6,638,508) teach that complexing of radio-labeled streptavidin to an anti-streptavidin antibody caused rapid localization of the complex to the spleen and liver reticulo-endothelial system and the uptake of antigen-antibody complexes via Fc receptors on macrophages (column 24, lines 15-25). Schechter et al states that "A complex between TNP-BSA and anti-TNP antibody was cleared away as expected for a normally degraded protein: 17% in the spleen and 9% in the liver at 3 h". Beatty et al (EP 327,746) teach that if an antibody is administered which binds to a substantial amount of marker substance in the circulation, then the antigen-antibody complexes will be cleared rapidly, primarily by the liver and spleen (page 2, lines 34-36). The abstract of Tromholt et al (Journal of Nuclear Medicine, 1991, Vol. 32, pp.

2318-2321) teaches that more than 99% of complexes of tissue plasminogen activator (t-PA) and anti-t-PA were removed by the liver within 10 minutes. Thus, it is well-known in the art that the presence of an antibody-antigen complex is rapidly eliminated from circulation via the reticulo endothelial system involving binding of the Fc domain of the antibody to the Fc receptors of the reticulo-endothelial system. The specification does not teach how to prevent the elimination of the instant antibody-antigen complexes from circulation in order to attain an increased half-life over the biotintylated chemokine as disclosed and a therapeutic effect. It is noted that the specification states on page 5, lines 20-21 that the invention includes Fab'2 fragments, however, anti-biotin Fab'2 when bound to the biotin conjugate of the instant invention would not be expected to contribute to an increased half-life relative to the biotintylated chemokine because the Fab'2 fragments are lacking the Fc domain which, when not part of an antigen-antibody complex, contributes to an increased half-life in vivo. One of skill in the art would be subject to undue experimentation in order to make complexes having an increased half-life and use the claimed complex to produce a therapeutic effect.

6. All other rejections and objections as set forth in the previous Office action are withdrawn.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10 a.m. to 9 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571)272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.
05/16/2004

Karen A. Canella
KAREN A. CANELLA PH.D
PRIMARY EXAMINER